

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<u>Africa</u>			
Institut Pasteur Place Charles-Nicollle Casablanca, Morocco	<u>Cerastes cerastes</u> <u>Vipera lebetina</u>	Antivipérin	
Institut Pasteur 13 Place Pasteur Tunis, Tunisia	<u>Cerastes cerastes</u> <u>Vipera lebetina</u>	Antivipérin	
Al Aigousa Sharea Alvezara Cairo, Egypt	<u>Cerastes cerastes</u> <u>Cerastes vipera</u> <u>Naja haje</u> <u>Cerastes cerastes</u> <u>Cerastes vipera</u>	Anti-Vipera  Polyvalent	
The South African Institute for Medical Research P.O. Box 1036 Johannesburg 2000 Republic of South Africa	<u>Hemachatus haemachatus</u> <u>Naja nivea</u> <u>Naja haje</u> <u>Naja melanoleuca</u> <u>Naja nigricollis</u> <u>Ondroaspis angusticeps</u> <u>Ondroaspis jensoni</u> <u>Ondroaspis polycephalus</u> <u>Bitis arietans</u> <u>Bitis gabonica</u> <u>Echis carinatus</u>	Polyvalent          Echis	Digested with pepsin and pre- cipitated with ammonium sulphate.

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Producers or Distributors	Venoms Used in Preparation	Trade or Common Name	Comments
Africa			
Fitz-Simon's Snake Park P.O. Box 1 Snell Parade Durban, South Africa	<u>Dendroaspis angusticeps</u>	Dendroaspis	Digested with pepsin, precipitated with ammonium sulphate, and dialyzed.
	<u>Dendroaspis jamesoni</u>		
	<u>Dendroaspis polylepis</u>		
	<u>Hemachatus haemachatus</u>	Polyvalent	
	<u>Naja nivea</u>		
<u>Bitis arietans</u> <u>Bitis gabonica</u>			
Middle East			
Ministry of Health Dept. of Laboratories P.O. Box 6115 Jerusalem 91060, Israel	<u>Echis coloratus</u>	Anti-Echis	Whole venom plus resin-bound "neurotoxin" used as antigen. Supplied as globulin fraction of horse serum in liquid form.
	<u>Vipera palaestinae</u>	Anti-Vipera	
Institut d'Etat des Sérum et Vaccins Razi P.O. Box 656 Teheran, Iran	<u>Naja naja oxiana</u>	Anti-Cobra	Prepared by pepsin digestion, and ammonium sulphate precipitation.
	<u>Vipera lebetina</u>	Anti-Lebetina	

(Continued)

(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<u>Middle East</u>			
	<u>Echis carinatus</u>	Anti-Echis	
	<u>Pseudocerastes persicus</u>	Anti-Persica	
	<u>Vipera xanthina</u>	Anti-Latif	
	<u>Agkistrodon halys</u>	Anti-Agkistrodon	
	<u>Naja naja oxiana</u>		
	<u>Vipera lebetina</u>		
	<u>Echis carinatus</u>		
	<u>Pseudocerastes persicus</u>	Polyvalent	
	<u>Vipera xanthina</u>		
	<u>Agkistrodon halys</u>		
<u>Asia</u>			
Haffkine Biopharmaceutical Corp., Ltd. Parel, Bombay India	<u>Bungarus caeruleus</u>	Polyvalent	Digested with pepsin, concentrated and lyophilized.
	<u>Naja naja</u>		
	<u>Vipera russelli</u>		
	<u>Echis carinatus</u>		
Central Research Institute Kasauli, India	<u>Naja naja</u>	Anti-Naja	Enzyme-refined globulin in liquid and lyophilized forms.
	<u>Bungarus caeruleus</u>	Anti-Bungarus	
	<u>Vipera russelli</u>	Anti-Vipera	

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Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
Asia			
	<u>Echis carinatus</u>	Anti-Echis	
	<u>Naja naja</u>		
	<u>Bungarus caeruleus</u>		
	<u>Vipera russelli</u>	Polyvalent	
	<u>Echis carinatus</u>		
National Institute of Health Biological Products Div. Islamabad, Pakistan	<u>Vipera russelli</u>	Monovalent Vipera	
	<u>Echis carinatus</u>	Monovalent Echis	
	<u>Naja sp.</u>		
	<u>Bungarus sp.</u>		
	<u>Vipera russelli</u>	Polyvalent Anti-snake Serum	
	<u>Echis carinatus</u>		
Industrie and Pharmaceutical Corporation Rangoon, Burma	<u>Naja n. kaouthia</u>	Mono-cobra	Precipitated with ammonium sulphate and lyophilized.
	<u>Vipera russelli siamensis</u>	Mono-Vipera	
	<u>Naja n. kaouthia</u>	Biovalent	
	<u>Vipera russelli siamensis</u>		
Queen Saovabha Memorial Institute Rama 4 Road Bangkok, Thailand	<u>Bungarus fasciatus</u>	Bungarus	
	<u>Naja naja</u>	Cobra	
	<u>Ophiophagus hannah</u>	King Cobra	

(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Asia</b>			
Perusahaan Umum Bio Farma (Pasteur Institute) Jl. Pasteur 20 P.O. Box 47 Bandung, Indonesia	<u>Vipera russelli</u>	Russell's Viper	Purified serum supplied in liquid form.
	<u>Agkistrodon* rhodostoma</u>	Malayan Pit Viper	
	<u>Trimeresurus albolabris</u>	Bivalent	
	<u>Trimeresurus erythrus</u>		
	<u>*Calloselasma</u>		
Shanghai Vaccine and Serum Institute 1262 Yang An Road Shanghai, China	<u>Agkistrodon halys</u>	Hamushi	Precipitated with ammonium sulphate and lyophilized.
	<u>Agkistrodon acutus</u>		
	<u>Agkistrodon</u>		
National Institute of Preventive Medicine 161 Kun-Yang Street Nan-Kang, Taipei Taiwan	<u>Agkistrodon acutus</u>	Agkistrodon	Immunized with formalin-toxoid venom. Ammonium sulphate precipitated, and supplied
	<u>Naja naja atra</u>	Naja Bungarus	
	<u>Bungarus multicinctus</u>		

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Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
Asia			
	<u>Naja naja atra</u> <u>Bungarus multicinctus</u>	"Polyvalent neuro-toxic antivenins"	in liquid or lyophilized form.
	<u>Trimeresurus mucrosquamatus</u> <u>Trimeresurus gramineus</u>	"Polyvalent haemorrhagic antivenin"	
The Chemo-Sero-Therapeutic Research Institute 668 Okubo Shimizu Kumamoto 860, Japan	<u>Trimeresurus flavoviridis</u> <u>Agkistrodon halys</u>	Habu Mamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Takeda Chemical Industries, Ltd. Higashi-Ku Osaka, Japan	<u>Agkistrodon halys</u>	Mamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Research Institute for Microbial Diseases Osaka University Kita-ku Osaka, Japan	<u>Agkistrodon halys</u>	Mamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.

(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<u>Asia</u>			
Kitasato Institute Minato-ku Tokyo, Japan	<u>Agkistrodon halys</u>	Mamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Chiba Serum Institute 2-6-1 Konodai, Ichikawa Chiba, Japan	<u>Agkistrodon flavoviridis</u> (absorbed habu toxoid) <u>Agkistrodon halys</u>	Habu Mamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Serum and Vaccine Laboratories Alabang Mutinlupa Rizal, Philippines	<u>Naja naja philippinensis</u>	Cobra	Concentrated and purified.

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<u>Australia</u>			
Commonwealth Serum Labs 45 Poplar Road Parkville, Victoria 3052 Australia	<u>Acanthophis antarcticus</u>	Death adder	Prepared by pepsin digestion, and ammonium sulphate precipitation. The products are dialyzed and ultra-filtered to a final concentration of 17% protein.
	<u>Notechis scutatus</u>	Tiger snake	
	<u>Enhydrina schistosa</u>	Sea snake	
	<u>Oxyuranus scutellatus</u>	Taipan	
	<u>Pseudonaja textilis</u>	Eastern brown snake	
	<u>Pseudechis australis</u>	Brown snake or Mulga	
<hr/>			
Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<u>Australia</u>			
	<u>Oxyuranus scutellatus</u>		
	<u>Acanthophis antarcticus</u>		
	<u>Notechis scutatus</u>	Polyvalent	
	<u>Pseudechis australis</u>	(Australia-New Guinea)	
	<u>Pseudonaja textilis</u>		



should show efficacy for 10 or more years, but the legal complications attending their use beyond five years make it necessary to advise that the antivenin be discarded or used for laboratory research purposes. A listing of antivenin producers is shown in Table II.

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## APPENDIX: GLOSSARY OF TERMS

ACQUIRED IMMUNITY: Immunologic resistance developed after birth as a result of previous exposure. Sometimes referred to as "specific active immunity".

ACTIVE IMMUNIZATION: Induction of a state of immunity, usually to a specific antigen, produced by the individual's or animal's own immune system.

ADJUVANT: A substance that can increase the specific production of an antibody to an antigen by increasing its size or length of survival in the circulation.

AFFINITY: The intrinsic binding power of an antibody-combining site with an antigenic substrate binding site.

AGGLUTINATION: Antigen-antibody reaction in vitro in which contact results in aggregates or clumps.

AGGLUTININ: A multivalent molecule that causes agglutination by direct interaction with its corresponding antigen. IgM is a particularly potent agglutinin.

ALLELE: An inherited variant of a gene.

ALLERGEN: A substance capable of inducing an allergic reaction.

ALLERGIC: A state of altered reactivity, generally denoting hypersensitivity.

ALLERGY: An immune reaction resulting in a reaction to some tissues or cells, usually through a hypersensitivity reaction.

ALLOGENIC: Having a different genetic constitution, usually used to describe intraspecies antigenic differences (xenogeneic).

**ALLOSTERIC TRANSFORMATION:** The binding of C1 to the antigen-antibody complex, resulting in a shape change that exposes a new site (allosteric site) by which it can react with another complement protein (C4).

**ALLOTYPE:** A genetic marker at an individual locus, usually inherited as alternatives.

**ANAPHYLAXIS:** A state of severe hypersensitivity to a foreign substance caused by the release of vasoactive amines, and triggered by the interaction of cell-bound antibody with the antigen.

**ANAPHYLOTOXINS:** Substances that degranulate mast cells on being released during an anaphylactic reaction. Histamine and serotonin are major anaphylotoxins.

**ANERGY:** Absence of immunological reactivity.

**ANTIBODY:** A molecule produced in response to exposure to an antigen and which has the property of combining specifically with that antigen at its antigen-combining site.

**ANTIGEN:** A substance of relatively high molecular weight that is capable of mitigating the production of an antibody specific to itself.

**ANTIVENIN (ANTIVENENE, ANAVENIN, ANTIVENIMEUX, ANTIVENINIUM, ANTIVENOM):** An antitoxin prepared by immunizing animals against a specific venom or venoms, processing the sera, and preparing it for use in humans or other animals. Antivenin is preferred to the other terms on the basis of historical precedent and the implication that it identifies a specific technique, that is, the immunization of animals. The term antivenom is frequently employed to denote any substance that has an action against a

venom, such as tannic acid, extracto de guaco,  $KMnO_4$ , strychnine, musk, or any other substance. Antivenin also enjoys a far more world-wide usage than the other words. For these reasons antivenin seems a more appropriate and less confusing term.

**ANTIVENIN INDEX:** A listing of the antivenins available in zoos and universities throughout the United States for the treatment of native and exotic snakes.

**ATTENUATED:** To be rendered less virulent.

**AUTOANTIBODY:** An antibody directed against self antigens (autoantigens).

**AVIDITY:** The combining power of an antibody with its antigen; related to the affinity and the valencies of the antibody and its antigen.

**BLOCKING ANTIBODY:** An "incomplete" antibody capable of coating the red cell determinant to render it partially or completely blocked and inagglutinable by antibodies of the same specificity.

**CAPPING:** The process of redistribution of cell-surface determinants to one small part of the cell surface.

**CARRIER:** An immunogenic molecule to which a hapten is coupled in such a way as to induce an immunological response.

**CLONE:** A family of cells or organisms of identical genetical constituents derived asexually from a single cell by repeated division.

**COBRA VENOM FACTOR (CVF):** A C3b analogue isolated from cobra venom. It has the property of activating the 'alternative pathway' of complement activating and destroying C3-C9.

**COLD AGGLUTININ:** An agglutinin whose optimum temperature of reactivity is in the cold, whose potency decreases with increases in temperature, and whose reaction at 37°C is usually negative.

**COMPLEMENT:** A complex group of 11 distinct glycoproteins found in the blood serum and other body fluids that react with one another sequentially in a cascading reaction to form potent biological effects, including immune adherence, phagocytosis and cell lysis. Complement factors are designated by the letter C: C1, C2, etc. C1 is composed of three subunits: C1q, C1r, and C1s. Activation of the complement system occurs with IgM or IgG. Chemically, these proteins are fairly large molecules, 75,000 - 240,000 daltons.

**COMPOUND ANTIGEN:** A combination of more than one antigen against which a single antibody appears to be directed.

**CYCLIC AMP:** An intracellular mediator having a particularly important effect on the activity of microtubules and other contractile elements of a cell.

**CYTOPHILIC:** Having an affinity for cells. Usually applied to antibodies which bind to macrophages.

**DOUBLE DIFFUSION:** Immunochemical analysis of antigenic relationships, pioneered by Ouchterlony.

**EFFECTOR CELL:** A cell actually carrying out a specific function, such as cell-mediated cytotoxicity.

**ELISA:** An acronym for enzyme-linked immunosorbent assay. This assay utilizes the principle of a solid phase (e.g., beads or microtiter plate wells) coated with antigen or antibody and an indicator reagent, antibody or antigen, respectively, to which an enzyme has been conjugated or "linked".



ENDOTOXIN: Lipopolysaccharides localized in cell walls.

EXOTIC SNAKES: Foreign, or those non-native to the United States.

Fab FRAGMENT: The fragment of the antibody molecule capable of antigen binding.

FREUND'S ADJUVANT: A water-oil emulsion of antigen-killed M. tuberculosis, usually in the oily phase (complete Freund's adjuvant). Incomplete Freund's adjuvant contains no organisms in the oil phase.

HAPTEN: A small molecule which will combine with antibody but which is not capable of evoking an antibody response in itself.

HEMAGGLUTININ: A molecule capable of agglutinating red blood cells.

HETEROLOGOUS: Usually used to denote inter-species antigenic differences.

IDIOTYPE: An antigenic marker for the antibody combining site. The antigen is found in the region of the antibody secreted by a single clone of lymphoid cells. Antibodies of different specificities have different idiotypes.

IgG: The predominant immunoglobulin class present in human serum.

IMMUNE ADHERENCE: A "glue-like" phenomenon occurring when a particulate antigen, its homologous antibody, and complement unite.

IMMUNITY: Resistance to extraneous, foreign matter as determined by the immune system.

IMMUNOCONGLUTININS: Antibodies (often autoantibodies) formed to complement components or their breakdown products, often autoantibodies.

**IMMUNOFLOURESCENCE:** The method involving the use of fluoro-chrome-labelled antibody to cellular determinants.

**IMMUNOGENIC:** Producing immunity. Antigenic.

**IMMUNOGENICITY:** The ability of an antigen to stimulate antibody production.

**IMMUNOGLOBULIN:** An antibody containing globulins, including those proteins without apparent antibody activity.

**IMMUNOLOGIC ENHANCEMENT:** The prolongation of the survival of an allograft from the action of a humoral antibody as against donor-histocompatible antigens that are lacking in the host.

**INCOMPLETE ANTIBODY:** An antibody that sensitizes red cells suspended in saline but fails to agglutinate them.

**INHIBITION:** The blocking of the normal reaction between an antigen and its corresponding antibody.

**ISOANTIBODY:** An antibody that reacts with an antigen present in another member of the same species but not in the animal itself.

**ISOANTIGEN:** An antigen that elicits antibody formation in another member of same species not genetically identical.

**MAJOR CROSSMATCH:** A compatibility test used to detect the presence of antibody in the recipient's serum: donor's red cells versus recipient's serum.

**MINOR CROSSMATCH:** A compatibility test used to detect the presence of antibody in the donor's serum: donor's serum versus recipient's red cells.

**MONOCLONAL:** Derived from a single-cell clone, usually immunoglobulin, to denote unusual homogeneity.

**MONOVALENT:** A single antigen or antibody. In general, monovalent antivenins are prepared with the venom of a single species of snake, although the antivenin may mitigate the effects of antigens of several or more snakes of the same or closely related genera.

**NATURALLY OCCURRING ANTIBODIES:** Antibodies that occur without an apparent stimulus. Also known as non-red-cell-immune antibodies or innate antibodies.

**PANAGGLUTINATION:** The reaction of red cells, irrespective of blood group, with all human sera.

**PASSIVE ANTIBODY:** An antibody which, when injected into an individual, provides temporary immunity.

**PHAGOCYTOSIS:** Ingestion of a solid or semisolid material into a cell by closing off an invagination of the protoplasm. The process requires the activity of contractile elements of the cells and aerobic respiration. The contents of the phagosome are usually digested by the discharge of cathepsins and other enzymes into the phagosome.

**PLASMA CELLS:** A terminally differentiated antibody-forming cell with a short half-life.

**POISONOUS ANIMAL:** Those creatures whose tissues, either in part or in their entirety, are toxic. Poisoning by these animals usually takes place through ingestion of their flesh. Sometimes called cryptotoxic animals.

**POLYAGGLUTINATION:** The agglutination of red cells by most human sera, irrespective of blood group.

**POLYVALENT:** Referring to several or many antigens or antibodies, often of different species, genera or even families.

**PRECIPITATION:** The reaction of soluble antigens with antibody, resulting in arcs or flocculation of the complexes in a gel medium.

**PRECIPITIN:** An antibody that reacts with its corresponding antigen to form a precipitate.

**PRIMARY RESPONSE:** The initial response to a foreign antigen.

**PSEUDOAGGLUTINATION:** The clumping of cells caused by agents other than antibodies.

**PYROGENS:** Thermostable, filter-passing substances that may cause febrile reactions when injected into a recipient. Probably of bacterial origin.

**REAGENT RED CELLS:** Red cells used in the laboratory for testing purposes.

**RIA:** A variety of immunological methods in which a radioactive isotope is used to detect antigens or antibodies.

**SALINE ANTIBODY:** An antibody that reacts with saline-suspended red cells.

**SENSITIZATION:** Stimulation by an antigen that renders a person liable to form antibodies.

**SPECIES-SPECIFIC:** Antigens or antibodies restricted to a particular species.

**SPECIFICITY:** The affinity between an antigen and its corresponding antibody.

**SUBGROUPS:** With respect to antigens or antibodies, subdivisions; often weakened forms.

**SYNERGISM:** The cooperative action between venom components.

**TOLERANCE:** A state of specific immunological unresponsiveness induced by exposure to antigen.

**TOXIN:** A substance derived from the tissues of a plant, animal, or microorganism which has a deleterious effect on another plant or animal. The word is usually used to denote a venom or poison fraction, although it is sometimes used to indicate the whole venom.

**TOXOID:** Toxins that have been modified to minimize their deleterious effects, while still retaining their immunogenic and antigenic properties.

**VACCINATION:** The inoculation or ingestion of organisms or antigens to produce immunity to those organisms or antigens in the recipient.

**VENOMOUS ANIMAL:** An animal having a venom gland or highly specialized group of secretory cells, a venom duct (although this is not a consistent finding), and a structure for delivering the venom, such as a sting, tooth or fang.

**WARM ANTIBODY:** An antibody that reacts optimally at 37°C.